REMARKS

Claims 1-18 were pending in the instant application. Claims 4, 13 and 18 have been canceled without prejudice or disclaimer, and claims 1-3, 5-12, 14-15, and 17 have been amended. Accordingly, claims 1-3 and 5-12, and 14-17 will be pending in the application upon entry of the instant Amendment.

Support for the amendments to the claims can be found in the specification at least, for example, at page 15, lines 11-14. No new matter has been added to the application by way of the amendments to the claims. For the Examiner's convenience, a clean copy of the claims that will be pending upon entry of the instant Amendment is annexed hereto as Appendix A.

Amendment and/or cancellation of the claims should in no way be construed as an acquiescence to any of the rejections set forth in the instant Office Action, and was done solely to expedite prosecution. Applicants reserve the right to pursue the claims as originally filed in this or one or more separate applications.

The title has been amended to more accurately reflect the amended claims. The specification has been amended to update the related application data originally entered into the application by amendment pursuant to item 4 on page 2 of the continuation application transmittal letter filed on November 21, 2001. In particular, patent numbers have been inserted where indicated.

Change of Address and Attorney Docket Number

Applicants have filed on even date herewith Notifications of Changes of Correspondence Address and Attorney Docket Number.

Claim Rejections - 35 U.S.C. §112, First Paragraph

Claims 1-18 are rejected under 35 U.S.C. §112, first paragraph, because the specification, although enabling for the recombinant strain of *Bacillus subtilis* YB886 (pLOI1500) transformed with *Z. mobilis* ADH and PDC genes, does not reasonably provide enablement for any eukaryotic cell or a method for ethanol production, including any animal cell, insect cell or fungal cell transformed with genes encoding ADH and PDC genes.

Applicants respectfully disagree and submit that the specification provides teachings and examples that would enable one of skill in the art to make and use the invention over the full scope claimed without undue experimentation.

In particular, the Examiner's attention is invited to the specification at page 14, line 2 through page 15, line 10, where Applicants describe in detail the chromosomal integration of foreign genes, in particular Z. mobilis *adh* and *pdc* genes. At page 15, line 11 through page 17, line 28, the specification provides detailed information about how to select a suitable host cell, including factors to be considered in selecting a host (page 15, lines 26-29) and criteria for selecting hosts to ferment oligosaccharides to ethanol (page 16, lines 1-6). In particular the Examiner's attention is invited to page 15, lines 18- 25 where Applicants teach:

> "Appropriate methodology for the introduction of foreign genes is available for each of these different types of hosts. According to the present invention, *pdc* and *adh* genes can be introduced into a variety of different hosts and expressed using a variety of promoters. It is well within the skill of a person trained in this field to use the descriptions provided herein to make these constructions. For example, *pdc* and *adh* genes can be readily inserted into plasmids which have different host ranges. These vectors are available from catalogs and are well known to those skilled in the art."

Section 112 only requires that the "specification contain a written description of the invention, and the manner and process of making and using it". Applicants have done this as is evident from the foregoing citations to the specification. Additionally, it is well settled that the disclosure of invention set forth by Applicants in their application must be given the presumption of correctness and operativeness by the PTO, and the only relevant concern of the PTO under the circumstances should concern the truth of the assertions contained in the application. The Examiner proffers nothing but conjecture to controvert the truth of Applicants' assertions in the specification.

The Examiner is concerned that no examples are provided of successfully manipulating various eukaryotic cell types, such that the experimentation left to the skilled artisan would be undue. First, Applicants point out that the specification provides a working example with *Bacillus* species. When this working example is considered by the skilled artisan, in light of the

rest of the disclosure of the application and in light of the state of the art at the time the application was filed, Applicants submit that the skilled artisan would be able to practice the invention as claimed without undue experimentation.

Moreover, Applicants assert that working examples are not required to enable the breadth of the pending claims and that there is no magical relation between the number of representative examples and the breadth of the claims. Contrary to what the Examiner suggests, Applicants need not provide working examples for every embodiment of the invention.

. The key question, then, is whether it would require undue experimentation to conduct Applicants' methods as broadly claimed. The Examiner appears to be unduly concerned about the fact that one of skill in the art will have to engage in experimentation to practice the full scope of the invention. However, enablement is not precluded by the necessity for some experimentation, and a considerable amount of experimentation is permitted. Indeed, Applicants point out in the specification that those skilled in the art will appreciate that a number of modifications can be made to the methods and materials exemplified therein and those modifications are well within the skill of a person trained in this field. Although one skilled in the art may have to engage in a considerable amount of experimentation to practice certain embodiments of the invention, such experimentation would not be unduly burdensome based on the teaching of the application, the high level of skill of the artisan, and the state of the art at the time the application was filed.

It is Applicants' position that based on the teachings of the specification that the Examiner acknowledges enables practice of the claimed method with the disclosed species, the skilled artisan would be able to make and use the claimed methods without undue experimentation. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 U.S.C. §101

Claims 1-18 are rejected under 35 U.S.C. §101 as containing subject matter coextensive with that of claims 1-18 of USPN 5,916,787. The Office Action indicates that this type of double patenting rejection may be overcome by amending the conflicting claims such that they are no longer coextensive in scope.

Accordingly, the claims have been amended to recite "eukaryotic cell" (*e.g.*, animal cells, insect cells, fungal cells, or yeast cells which are not naturally ethanologenic) as opposed to "Gram-positive bacterium". Support for the amendment to the claims can be found in the specification at least, for example, at page 15 (lines 11-14) in a section entitled "Host selection" which states, in part, that the "range of organisms suitable for modification to express heterologous *pdc* and *adh* genes...includes, *inter alia*, eukaryotic cells, such as animal cells, insect cells, fungal cells, yeasts which are not naturally ethanologenic, and non-ethanologenic bacteria."

In view of the amendments described above, Applicants submit that that the claims, as presented herein, are no longer coextensive with the claims of U.S. Patent 5,916,787 which are particularly drawn to only those cells which are Gram-positive bacteria and not other types of cells. Accordingly, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. §101 are respectfully requested.

Non- Statutory Double Patenting

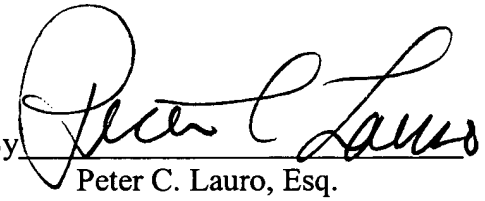
Claims 1-8 are rejected under the judicially created doctrine of double patenting over claims 1 and 2 of U.S. Patent 5,482,846. Applicants note the rejection and will address the rejection upon an indication that the application is in condition for allowance but for the non-statutory double patenting rejection.

CONCLUSION

In view of the foregoing, entry of the amendments and remarks herein, reconsideration and withdrawal of all rejections, and allowance of the instant application with all pending claims are respectfully solicited. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' attorney at the telephone number below.

Respectfully submitted,

EDWARDS & ANGELL, LLP

By 

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Date: January 27, 2004

Attachment: Appendix A – Clean Copy of the Claims That Will Be Pending

Appendix A

1. A eukaryotic cell which has been transformed with heterologous genes encoding alcohol dehydrogenase and pyruvate decarboxylase wherein said genes are expressed at sufficient levels to confer upon said cell transformant the ability to produce ethanol as a fermentation product.

2. The eukaryotic cell according to claim 1, wherein said cell is selected from the group consisting of animal cells, insect cells, fungal cells, and yeast cells.

3. The eukaryotic cell according to claim 2, wherein said cell is a fungal cell.

5. The cell according to claim 1, which has been transformed with *Z. mobilis* genes encoding alcohol dehydrogenase and pyruvate decarboxylase.

6. The cell according to claim 1, wherein said cell is further transformed with a gene encoding an enzyme which degrades oligosaccharides.

7. The cell according to claim 6, wherein said enzyme which degrades oligosaccharides is a polysaccharase.

8. The cell according to claim 7, wherein said polysaccharase is selected from the group consisting of cellulolytic, xylanolytic, and starch-degrading enzymes.

9. The cell according to claim 1, wherein said heterologous genes are incorporated onto the chromosome of said cell.

10. A method for the production of ethanol, said method comprising transforming a eukaryotic cell with heterologous genes encoding pyruvate decarboxylase and alcohol dehydrogenase wherein said genes are expressed at sufficient levels to result in the production of ethanol as a fermentation product.

11. The method, according to claim 10, wherein said cell is selected from the group consisting of animal cells, insect cells, fungal cells, and yeast cells.

12. The method, according to claim 11, wherein said cell is a fungal cell.

14. The method, according to claim 10, wherein said cell has been transformed with Z. *mobilis* genes encoding alcohol dehydrogenase and pyruvate decarboxylase.

15. The method, according to claim 10, wherein said cell is further transformed with a gene encoding an enzyme which degrades oligosaccharides.

16. The method, according to claim 15, wherein said enzyme which degrades oligosaccharides is a polysaccharase.

17. A method for reducing the accumulation of acidic metabolic products in the growth medium of a eukaryotic cell, said method comprising transforming said cell with heterologous genes which express alcohol dehydrogenase and pyruvate decarboxylase at sufficient levels to result in the production of ethanol as a fermentation product.